

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
20 October 2005 (20.10.2005)

PCT

(10) International Publication Number
WO 2005/097086 A3

(51) International Patent Classification:
A61K 31/515 (2006.01) **A61P 35/00** (2006.01)

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number:
PCT/US2005/011046

(22) International Filing Date: 1 April 2005 (01.04.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/558,889 2 April 2004 (02.04.2004) US
60/625,479 4 November 2004 (04.11.2004) US
60/658,745 4 March 2005 (04.03.2005) US

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicants and

(72) Inventors: **ROBBINS, Joan, M.** [US/US]; 10265 Pinetree Dr., San Diego, CA 92131 (US). **CANTWELL, Mark, J.** [US/US]; 11525 Caminito La Bar, #50, San Diego, CA 92126 (US).

(74) Agents: **PRESTON, David, R.** et al.; David R. Preston & Associates, 12625 High Bluff Drive, Suite 205, San Diego, CA 92130 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:

18 May 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/097086 A3

(54) Title: USE OF 5,10-METHYLENE TETRAHYDROFOLATE FOR THE TREATMENT OF CANCER

(57) Abstract: The present invention provides novel uses and compositions for 5,10-methylene tetrahydrofolate ("5,10-CH₂-THFA") in the treatment of cancer. The present invention is based on the surprising result that 5,10-CH₂-THFA, while increasing the efficacy of 5-fluorouracil (5-FU) in reducing the rate of tumor growth and increasing survivorship, also reduces the toxicity to the patient of 5-FU. The present invention provides methods and compositions for treating cancer patients that include 5-FU, 5,10-CH₂-THFA, and one or more additional anticancer drugs. Such methods and compositions can provide increased efficacy and reduced toxicity when compared with current treatment modalities.